REMARKS

Claims 1-3, 12, 13, 16-21, 34-35 and 41-43 are pending. Applicant notes that all amendments and cancellations of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the amended or cancelled Claims (or similar Claims) in the future. The Claims have been amended to recite a process and products made by a process where a population of cells enriched for umbilical cord matrix stem cells is made by (a) enzymatically dispersing umbilical cord matrix obtained from an umbilical cord to provide a fraction of cells comprising umbilical cord matrix stem cells, (b) exposing the fraction with umbilical cord matrix stem cells to conditions suitable for stem cell proliferation and (c) passaging said fraction with umbilical cord matrix stem cells to remove non-adherent cells and select a fraction of cells enriched for umbilical cord matrix stem cells, wherein said cells are negative for CD34 and CD45, positive for telomerase activity, proliferate in an in vitro culture for over one year, maintain a karyotype in which all the chromosomes of the human are present and not noticeably altered through prolonged culture, and maintain the potential to differentiate. Support for the enzymatically dispersing step may be found in the specification, for example at page 22, lines 23-24. Support for the remaining amendments may be found in the claims as originally filed. Applicants have replaced the color drawing with black and white drawings. The attached sheets of "Replacement Drawings" include Figures 12-16, 20A-D, 23A-D, 26, 28A-D and 30. Applicants wish to note that there is no new matter.

Applicants thank Examiner Ton for the telephonic interview on October 28, 2008 with inventors Mark Weiss and Kathy Mitchell and licensee Chris Drescher and the applicant's undersigned representative. In particular, the Applicants discussed the rejection over Purchio and differences between the methods described in the present specification and those used by Purchio. The Examiner recommended that Applicants submit data that show that the cell population obtained by the process differ from the Purchio prechondrocytes and from the Wharton's Jelly used by Purchio. Applicants further discussed the enablement and written

description rejections and the fact that Examples 8 and 9 disclose the use of the claimed populations of cells as opposed to clonal cell lines. Applicants have incorporated the remarks and amendments discussed during the interview into the claims and are pleased to present data in the accompanying Declaration of Dr. Kathy Mitchell (the "Mitchell Declaration") that is relevant to the rejections.

1. Claims 1, 3, 12, 13, 16-21, 34-35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement;

2. Claims 1, 3, 12, 13, 16-21, 34-35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement;

3. Claims 3, 34, and 35 stand rejected under 35 U.S.C. §102 as allegedly being anticipated by Purchio et al. (U.S. Pat. No. 5,919,702).

These rejections are addressed in order below.

1. The claims are enabled.

Claims 1, 3, 12, 13, 16-21, 34-35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The claims have been amended to refer to populations of cells that are enriched for umbilical cord matrix stem cells. Applicants respectfully submit that this amendment moots the Examiner's arguments supporting the enablement rejection. In particular, while the Examiner argues that "the specification fails to provide guidance for UCMS cells as a particular cell type," the Examiner admits that the specification "provides guidance for this cell in a composition including other cells." Office Action, p. 6. The claims now specifically refer such compositions, i.e., populations of cells enriched for UCMS cells.

The Examiner makes several arguments with respect enablement. Each of these arguments is addressed in turn.

At page 5 of the Office Action, the Examiner states that "the specification does not provide guidance for an enabled use of heterogeneous cell populations . . . . The uses that are contemplated in the specification are solely for UCMS cells, not heterogeneous populations, or compositions that comprise these cells." Applicants respectfully disagree. The Examiner's attention is directed to the Examples which demonstrate many uses for the claimed cell populations. Since the Examiner has admitted that the specification teaches how to obtain these populations and the Examples use those populations, the use of the cell population comprising UCMS cells is enabled. Example 1 teaches that the populations of cells can be used to make neuronal cells and that the populations are a source of neural stem cells. Example 5 contains additional data demonstrating that the populations of cells containing UCMS cells can be used to make a source of neural stem cells and neuronal cells. Example 8 contains data showing that the claimed populations of cells comprising UCMS cells can be transplanted into the brains of rats, do not stimulate an immune response, survive for many weeks, and differentiate into neural cells. Example 9 contains data demonstrating that populations of cells containing human UCMS cells can be transplanted into the brains of rats that model Parkinson's disease and that transplanted cells have a substantial benefit on the behavior of the rats. Thus, the production and use of the claimed populations of cells is well-established in the specification to one of ordinary skill in the art. This satisfies the standard for enablement, which requires that the specification show how to make and use the claimed invention.

At the bottom of page 5 of the Office Action, the Examiner argues further that "although the specification teaches expression of various markers, such a c-kit or alkaline phosphatase, however, it appears that these cells were found in a heterogeneous population of cells, and it is unclear if these cells/colonies expressed both markers simultaneously." The Examiner further argues on page 6 of the Office Action that "the claims require obtaining UCMS cells." The amendments to the claims moot this issue as the claims are now directed to populations of cells comprising UCMS cells and the population is defined by the method used to obtain the population of cells. As discussed in the Mitchell Declaration at ¶¶ 4-8, these process steps result in a population of cells that is distinguishable from Wharton's jelly cells. The Mitchell Declaration describes in detail how the cells produced by the claimed process steps provide a cell

population with distinct characteristics. Mitchell Declaration at ¶¶ 4-11. The specification teaches how to make and use such cell populations, such as in Examples 8 and 9. Mitchell Declaration ¶¶ 12 and 13. The claims require obtaining a population of cells that comprise UCMS cells. This is clearly taught in the specification.

On page 6, the Examiner states that "certain embodiments require that cells be capable of differentiation to cell types of all three germ layers (see, for example, claims 34 and 41). The claims have been amended to specify that the cells maintain the ability to differentiate. Thus, this argument by the Examiner is moot.

For the forgoing reasons, Applicants request that the enablement rejection be withdrawn.

2. The claims have an adequate written description.

Claims 1, 3, 12, 13, 16-21, 34-35, and 41-43 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. On page 7 of the Office Action, the Examiner states that "there is no guidance in the working examples with regard to the particular, identifying characteristics of a UCMS cell, only to a population of cells which comprise UCMS cells (i.e., a heterogeneous population of cells)." Emphasis Examiner's. Applicant's respectfully disagree with the Examiner's assertion that the specification does not provide particular, identifying characteristics of a UCMS cell. The specification provides many examples of identifying characteristics of UCMS cells, including expression of markers, morphology and the ability to differentiate into particular cell lineages as detailed in Applicant's previous response. Nevertheless, Applicants note that the Examiner has recognized that the working examples provide written description for a population of cells which comprise UCMS cells. The claims have been amended accordingly to refer to populations of cells that comprise UCMS cells. The Examiner further argues that "the as-filed disclosure fails to provide a written description for the claimed UCMS cells, and as such, there is no indication that Applicant's had possession of the claimed invention."

Applicants respectfully submit that the specification and the Examples discussed in regards to enablement demonstrate to a person of skill in the art that the Applicants had possession of a population of cells comprising UCMS cells as presently claimed. The

specification further demonstrates that the inventors had possession of the claimed invention and that a person of skill in the art would recognize the populations of cells made as claimed. As detailed in the Mitchell Declaration:

> A person of ordinary skill in the art would recognize that the specification teaches method to obtain the populations of cells used in the working examples, such as Examples 7 and 8. A person of skill in the art could obtain these populations of cells as described and use them in the described method. Accordingly, a person of skill in the art would conclude that we had possession of the claimed invention because the population of cells can be obtained as described in the specification and used as described. The person of skill in the art would further recognize that the cells obtained by the process will have the characteristics of the population as described in the specification.

Mitchell Declaration ¶ 13. Applicants further note that as discussed above, the Mitchell Declaration establishes that the claimed process steps result in a population of cells that is distinguishable from Wharton's jelly cells. Mitchell Declaration ¶¶ 4-8.

Applicants further note that the MPEP specifically approves product-by-process claims: "A product-by-process claim, which is a product claim that defines the claimed product in terms of the process by which it is made, is proper. *In re Luck,* 476 F.2d 650, 177 USPQ 523 (CCPA 1973); *In re Pilkington,* 411 F.2d 1345, 162 USPQ 145 (CCPA 1969); *In re Steppan*, 394 F.2d 1013, 156 USPQ 143 (CCPA 1967)." MPEP 2173.05(p).

Finally, with respect to the Examiner's arguments regarding differentiation into multiple cells types is moot in view of Applicant's amendments to the claims. Accordingly, Applicants request that the written description rejection be withdrawn.

3. The claims are not anticipated.

Claims 3, 34, and 35 stand rejected under 35 U.S.C. §102 as allegedly being anticipated by Purchio et al. (U.S. Pat. No. 5,919,702). The Examiner states that Purchio teaches cultures of Wharton's Jelly cells that can be cultured and expanded. Applicant's note that Purchio et al. (U.S. Pat. No. 5,919,702) have isolated chondrogenic progenitor cells (or prechondrocytes) from Wharton's Jelly. They reported the isolation of cells from human umbilical cord Wharton's Jelly

by removing blood, blood vessels and the amnion lining of the umbilical cord followed by and incubating the tissue under conditions purported to allow the prechodrocytes to migrate from Wharton's jelly explants and to proliferate. As such, the method did not distinguish the desired cells from the different cell types present in Wharton's Jelly nor those present in the entirety of the umbilical cord matrix, but rather relied on migration from the tissue or selecting growth conditions favoring prechondrocytes. The prechondrocytes were expanded mitotically after they were established. Cells at passages 2 to 4 were reported as useful to produce cartilage, if triggered by the addition of exogenous growth factors, such as BMP-13 or TGF-beta. Uses of the cells for direct injection or implantation, or use with a hydrogel or tissue matrix, were proposed. However, it was considered important that the cells not exceed about 25% confluence. The cells were not characterized with respect to their biochemical or immunological properties, or with respect to their gene expression.

Applicants respectfully submit that the current claim amendments to claims 3, 34, and 35 render this rejection moot. The composition claims have been amended to specify that a population of cells that are obtained by a three step process. The cell population obtained by this process is easily distinguishable both from unprocessed Wharton's jelly and the Purchio et al., prechondrocytes. The method of the current claim isolates cells **that are not** contained with the Purchio method. Purchio simply relies on migration of cells specifically from the Wharton's jelly. The claimed method enzymatically treats the entire matrix and therefore we isolate cells that arguably **cannot be isolated from the Purchio method**. Detailed data on this issue is presented in the Mitchell Declaration at ¶¶ 4-11 and in particular ¶ 8. As detailed in the Mitchell Declaration, the cell population obtained by the claimed process steps is different from the Purchio method prechondrocytes isolated from Wharton's jelly cells in terms of cell surface markers, morphology, and differentiation potential.

With respect to the claims as amended, Applicants must respectfully disagree with the assertion by the Office that on page 9 of the Action that "because Purchio teach a culture of cells from the same source as the instantly claimed cell compositions, Purchio's culture would inherently contain the cell compositions and cultures as instantly claimed." The Office has not established any reasonable basis on the present record demonstrating that the cells described by

Purchio et al. are the cell populations or contain the cell populations as made the process as presently claimed. Moreover, the Office has not established any reasonable basis on the present record demonstrating that the cells described by Purchio are the cells recited by the present claims in view of the difference between the methods by which the cells were obtained. The Mitchell Declaration clearly establishes that they are not and supports the contention that the complex structure of the umbilical cord would make it such that methodology of cell isolation from the umbilical cord would, in fact, result in different cells. The argument that *any* culture of Wharton's jelly would *inherently* contain the cells of the Weiss invention is not substantiated by prior art of Purchio. In addition, we have demonstrated by practicing both the art of the invention of Purchio et al., and Weiss et al., that the cells are *not* identical in terms of cell surface markers, morphology and differentiation potential.

Accordingly, Applicants request that the anticipation rejection be withdrawn.

CONCLUSION

Applicants believe that the claims are in condition for allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: October 30, 2008

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